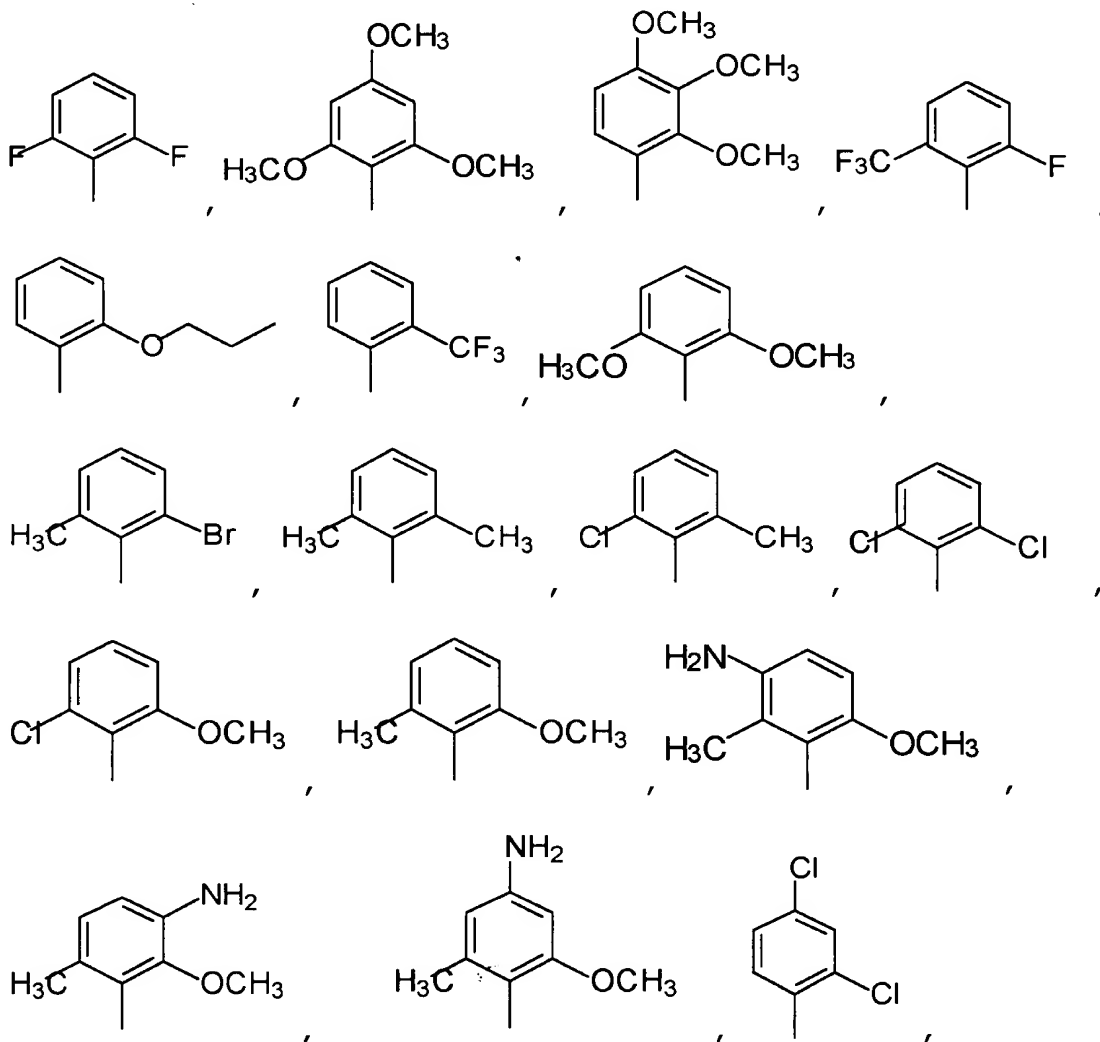
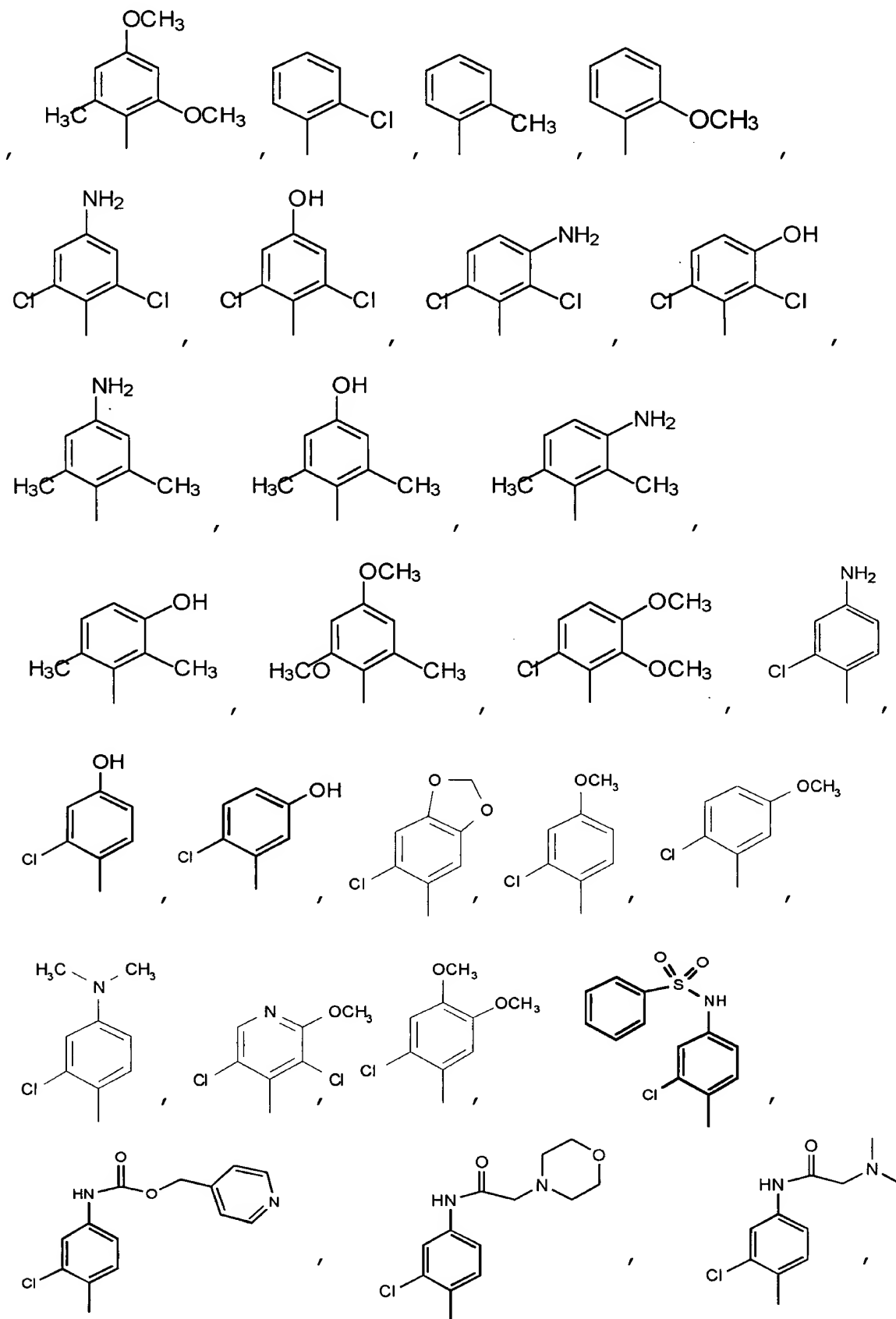


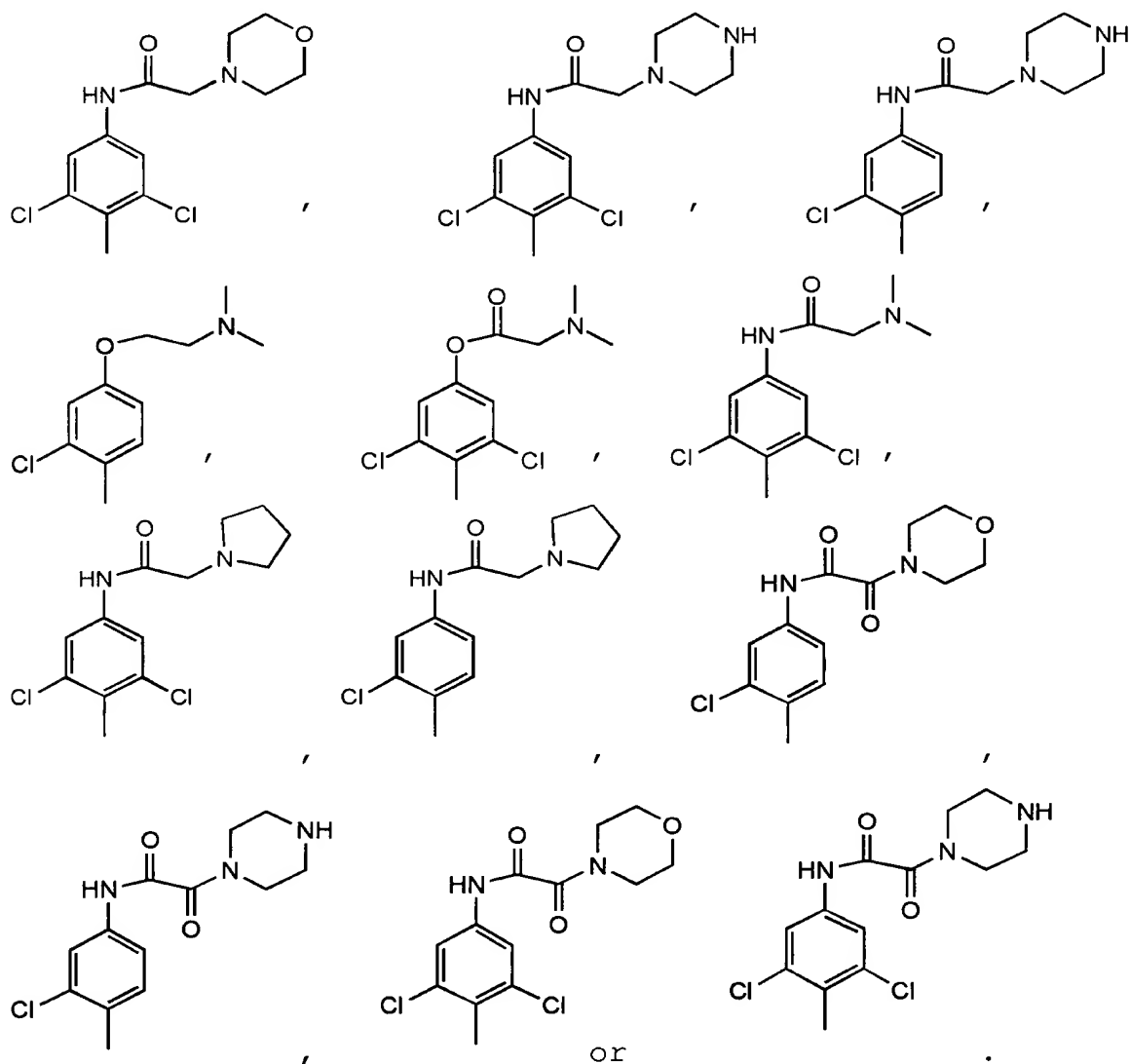
4 (Amended) The compound according to claim 4, wherein Q<sub>1</sub> is selected from:



B<sup>2</sup>



B



B<sup>3</sup> 9. (Twice amended) The compound according to claim 38, wherein X is selected from -S-, -O-, -S(O<sub>2</sub>)-, -S(O)-, -NR<sup>2</sup>-, -C(R<sup>2</sup>)<sub>2</sub>- or -C(O)-.

B<sup>4</sup> 18. (Twice amended) The compound according to claim 38, wherein Q<sub>3</sub> substituted with 2 to 4 substituents,

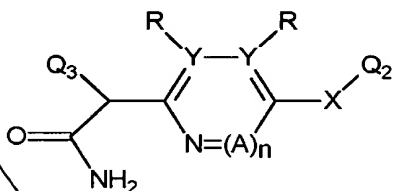
122

B

wherein at least one of said substituents is present in the ortho position relative to the point of attachment of Q<sub>3</sub> to the compound.

21. (Amended) The compound according to claim 19, wherein Q<sub>3</sub> contains 1 to 2 substituents in addition to said ortho substituents, said additional substituents being independently selected from NR'<sub>2</sub>, OR', CO<sub>2</sub>R', CN, N(R')C(O)R<sup>4</sup>; N(R')C(O)OR<sup>4</sup>; N(R')C(O)C(O)R<sup>4</sup>; N(R')S(O<sub>2</sub>)R<sup>4</sup>; N(R')R<sup>4</sup>; N(R<sup>4</sup>)<sub>2</sub>; OR<sup>4</sup>; OC(O)R<sup>4</sup>; OP(O)<sub>3</sub>H<sub>2</sub>; or N=CH-N(R')<sub>2</sub>.

22. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ie:

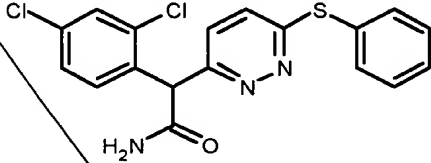
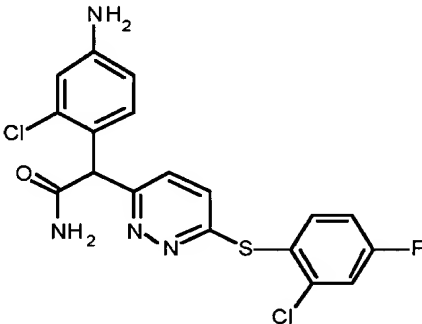
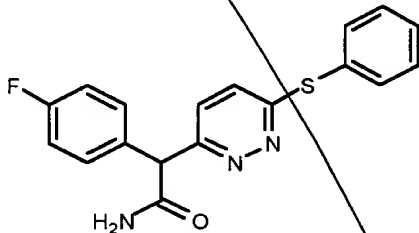
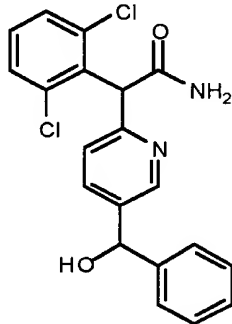
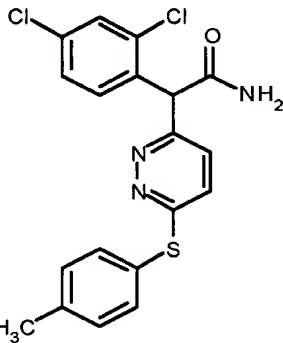
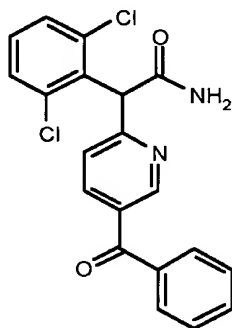


and is selected from any one of the following compounds:

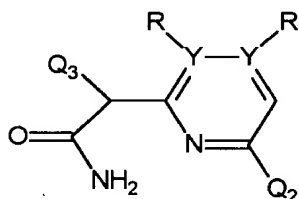
cpd #	structure	cpd #	structure
201		206	

B

*Sub C3 Cont*

cpd #	structure	cpd #	structure
203		207	
204		208	
205		209	

23. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ig:



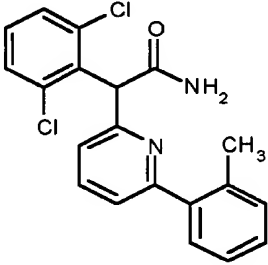
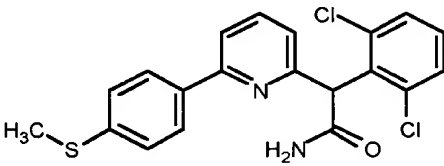
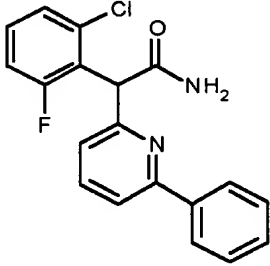
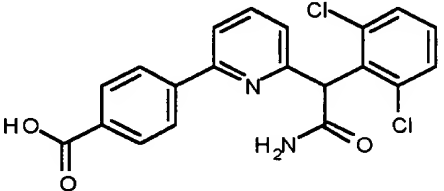
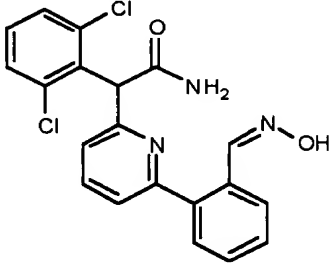
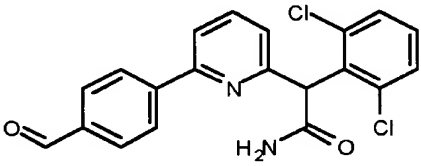
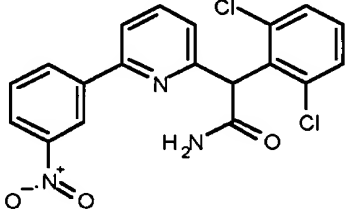
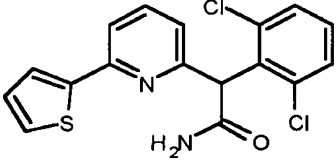
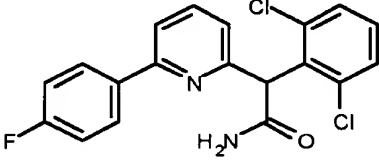
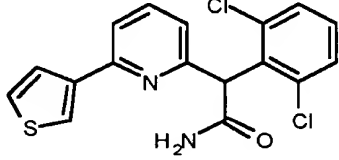
and is selected from any one of the following compounds:

*B*

cpd #	structure	cpd #	structure
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302		311	
303		312	
304		313	

Sub  
C3  
Cont

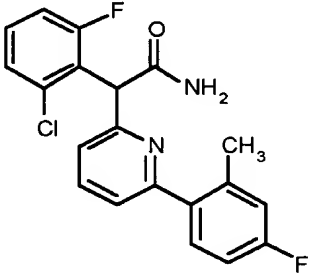
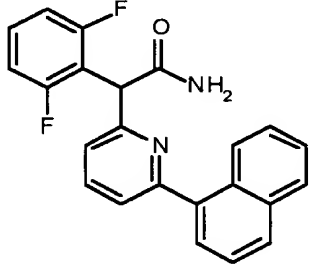
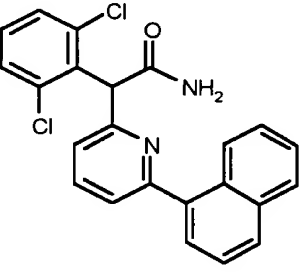
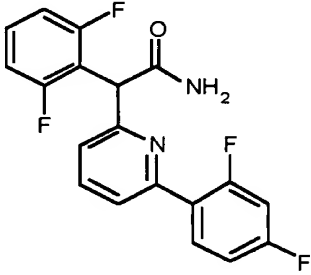
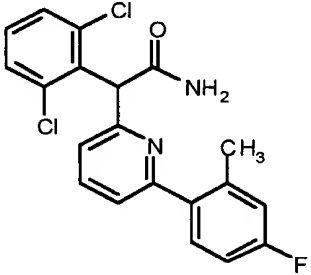
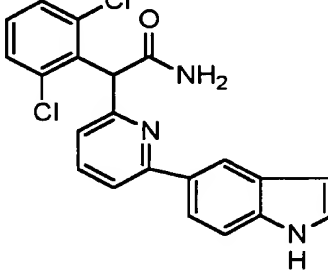
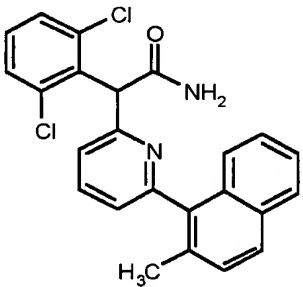
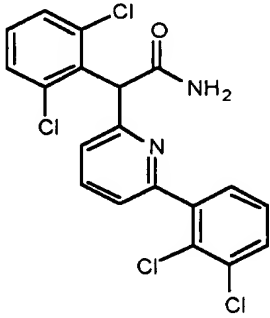
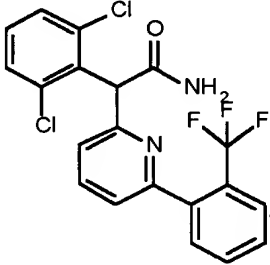
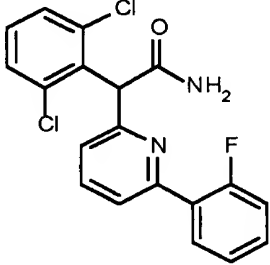
B

305		314	
306		315	
307		316	
308		317	
309		318	

Sub  
C3  
Cont

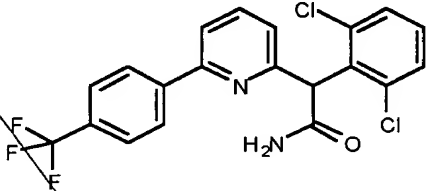
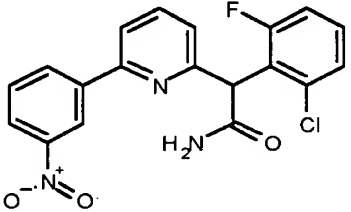
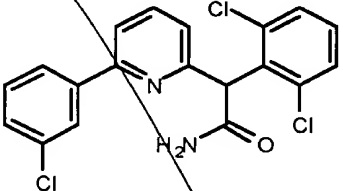
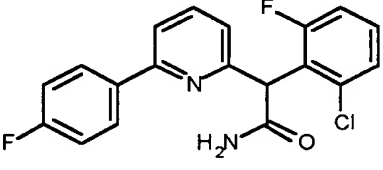
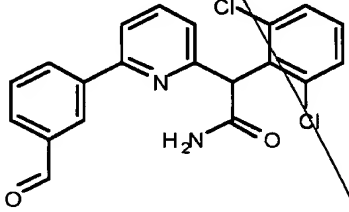
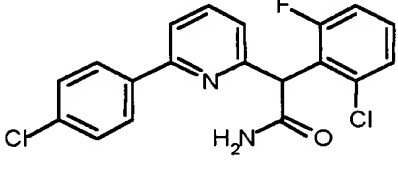
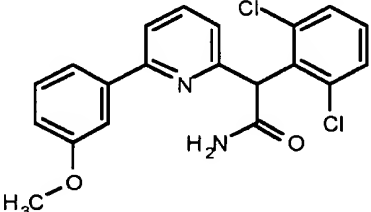
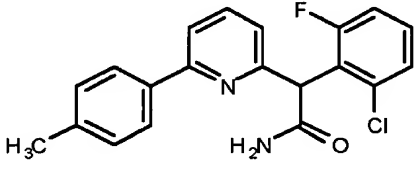
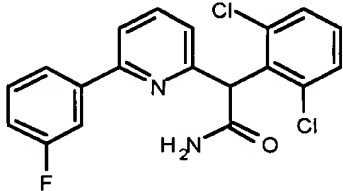
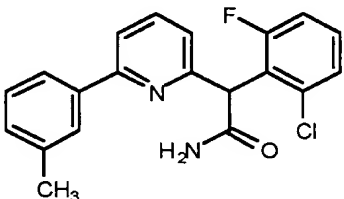
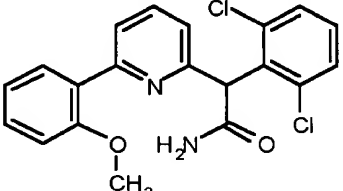
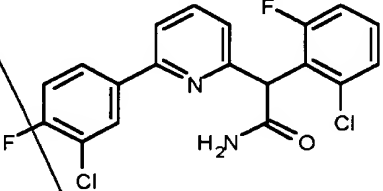
B

85  
sub  
C3  
cont

361		370	
362		371	
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373		382	
374		383	

B



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323		332	
324		333	

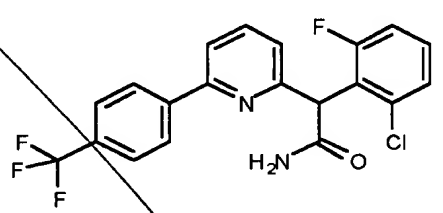
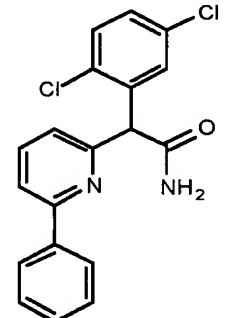
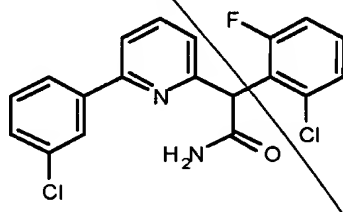
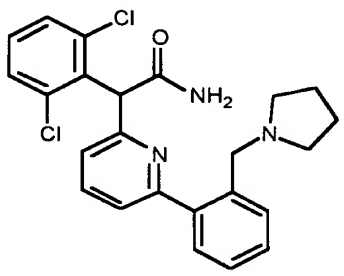
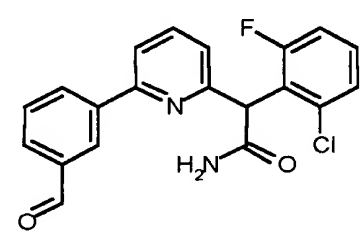
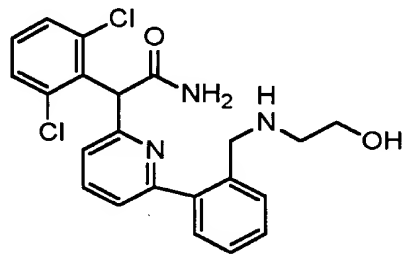
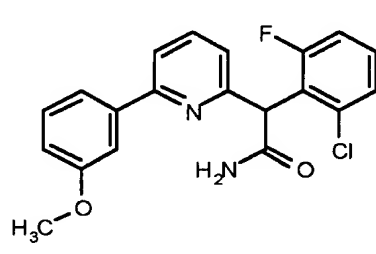
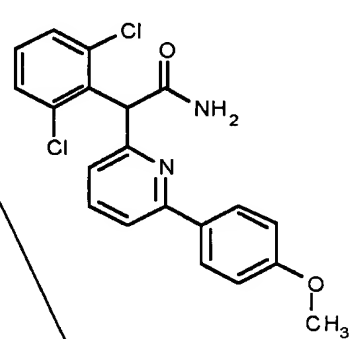
Sub  
C<sup>3</sup>

B

325		334	
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338		347	
339		348	

Sub  
C3

B

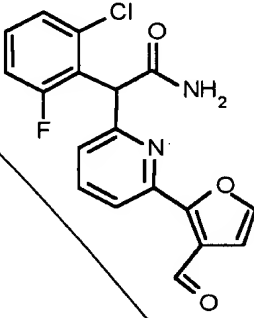
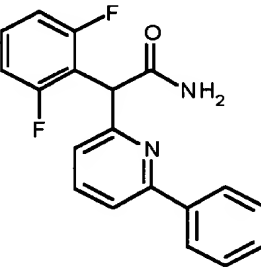
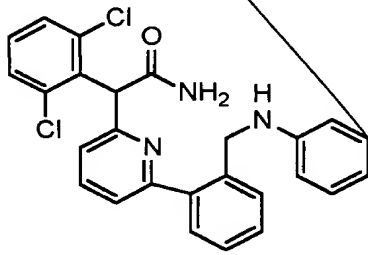
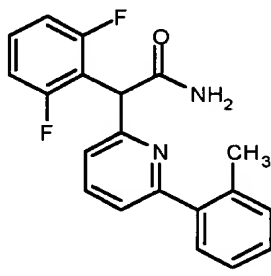
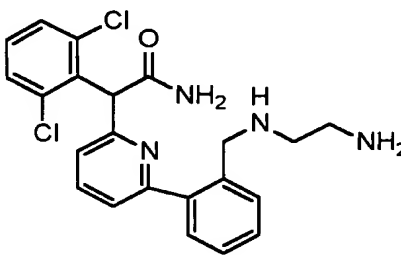
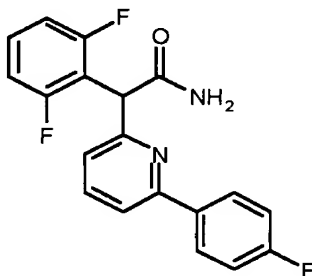
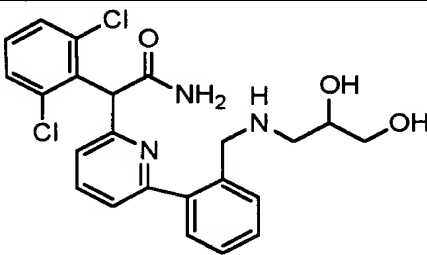
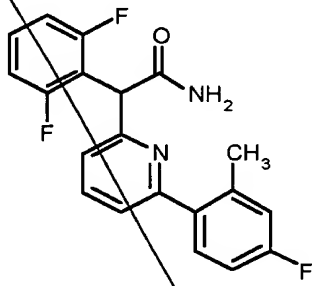
<p>340</p>		<p>349</p>	
<p>341</p>		<p>350</p>	
<p>342</p>		<p>351</p>	
<p>343</p>		<p>352</p>	

B

~~Sub~~  
C3

344		353	
345		354	
355		364	
356		365	

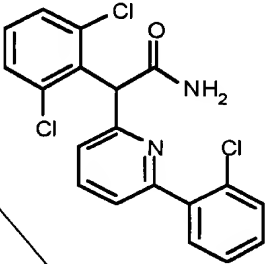
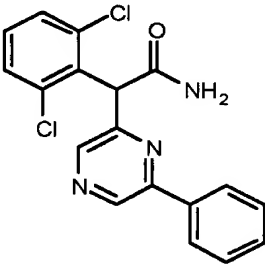
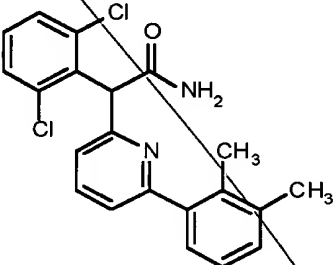
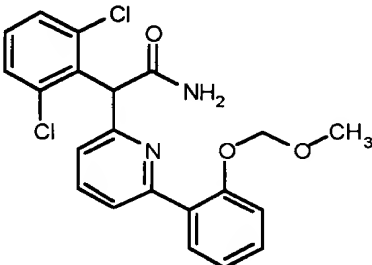
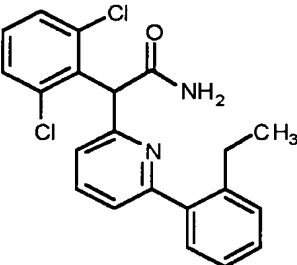
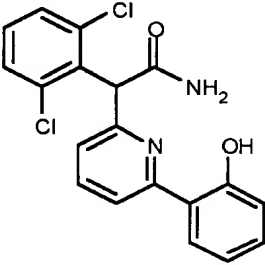
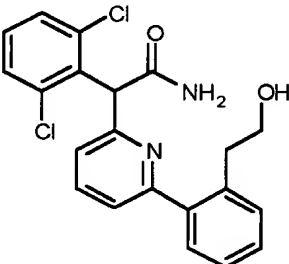
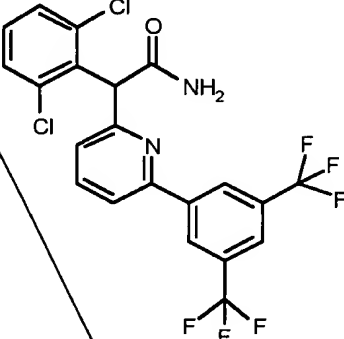
B

357		366	
358		367	
359		368	
360		369	

BS  
sub  
C3  
cont

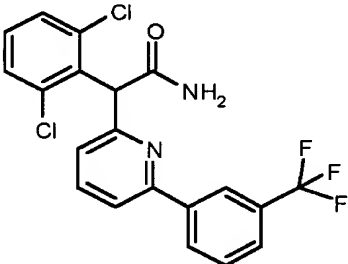
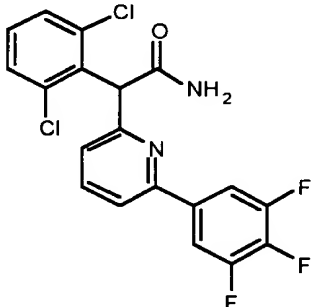
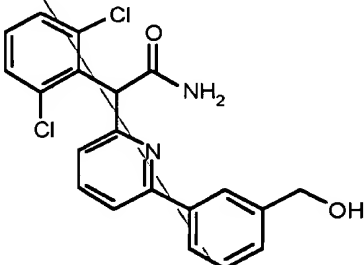
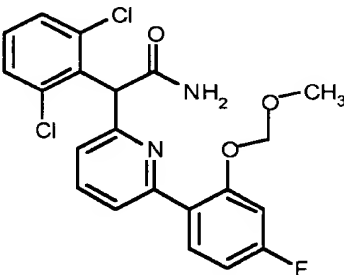
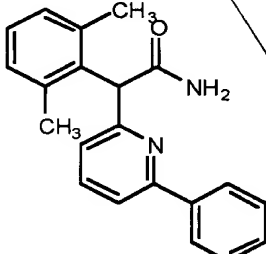
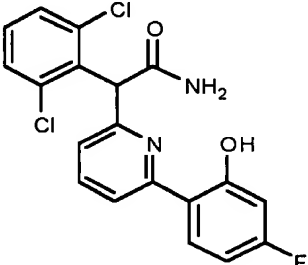
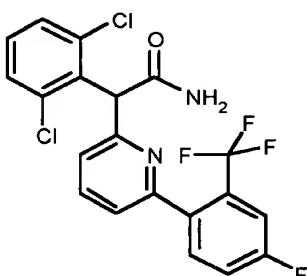
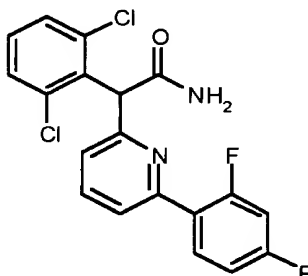
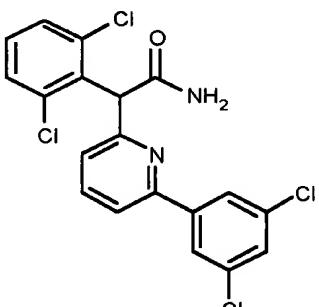
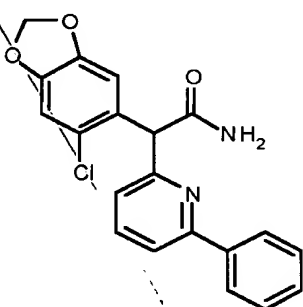
B

Sub  
C3  
cont

375		384	
376		385	
377		386	
378		387	

B

BS  
Sub  
C3  
cont

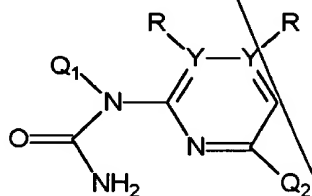
379		388	
380		389	
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391		396	
392		397	

B

~~Sub~~  
C3  
cont

393		398	
394		399	
395		1301	

24. (Twice amended) The compound according to claim 38, wherein said compound is a compound of formula Ih:

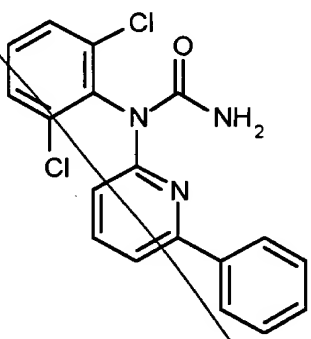
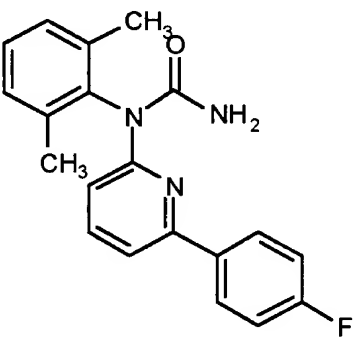
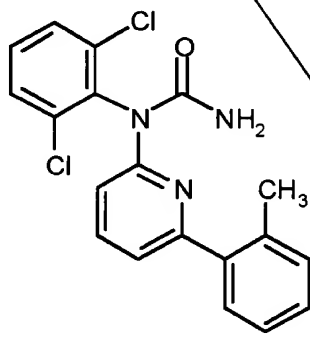
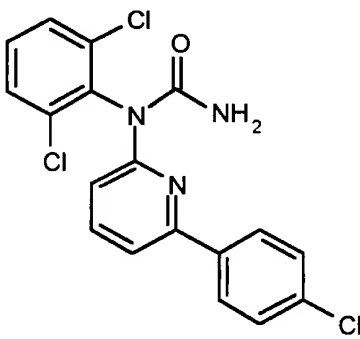
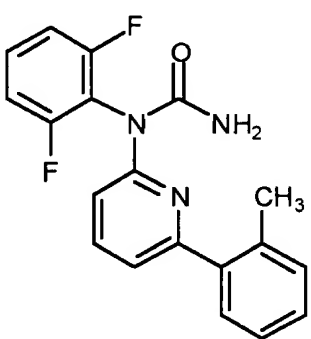
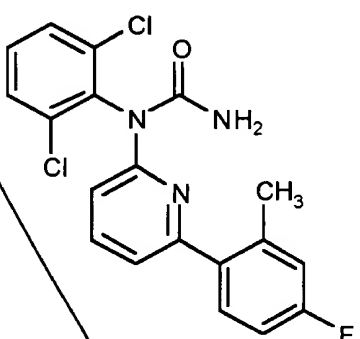


and is selected from any one of the following compounds:

B



~~Sub~~  
C3  
cont

cpd #	structure	Cpd #	structure
401		407	
402		408	
403		409	

B

Sub  
C3  
cont

cpd #	structure	Cpd #	structure
404		410	
405		411	
406		412	

26. A method of treating inflammatory diseases, autoimmune diseases, viral diseases, destructive bone disorders, proliferative disorders, infectious diseases, neurodegenerative diseases, reperfusion/ischemia in stroke, myocardial ischemia, renal ischemia, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin-induced platelet aggregation or

B6

Sub  
F1

B

B<sup>6</sup> [ conditions associated with prostaglandin endoperoxide synthase-2 in a patient, said method comprising administering to said patient a composition according to claim 25.

21  
27. (Amended) The method according to claim <sup>20</sup>26, wherein said method is used to treat an inflammatory disease selected from acute pancreatitis, chronic pancreatitis, asthma, allergies, or adult respiratory distress syndrome.

Sub F2  
28. (Amended) The method according to claim 26, wherein said method is used to treat an autoimmune disease selected from glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

Sub C4  
29. (Amended) The method according to claim 26, wherein said method is used to treat a destructive bone disorders selected from osteoarthritis, osteoporosis or multiple myeloma-related bone disorder.

30. (Amended) The method according to claim 26, wherein said method is used to treat a proliferative disease selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, or multiple myeloma.

L 31. (Amended) The method according to claim 26,

B<sup>6</sup> wherein said method is used to treat an infectious disease selected from sepsis, septic shock, or Shigellosis.

32. (Amended) The method according to claim 26, wherein said method is used to treat a viral disease selected from acute hepatitis infection, HIV infection or CMV retinitis.

33. (Amended) The method according to claim 26, wherein said method is used to treat a neurodegenerative disease selected from Alzheimer's disease, Parkinson's disease, cerebral ischemia or neurodegenerative disease caused by traumatic injury.

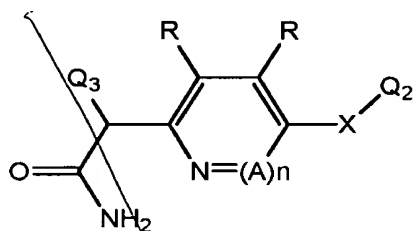
Sub F<sub>3</sub> 34. (Amended) The method according to claim 26, wherein said method is used to treat ischemia/reperfusion in stroke or myocardial ischemia, renal ischemia, heart attacks, organ hypoxia or thrombin-induced platelet aggregation.

35. (Amended) The method according to claim 26, wherein said method is used to treat a condition associated with prostaglandin endoperoxide synthase-2 selected from edema, fever, analgesia or pain.

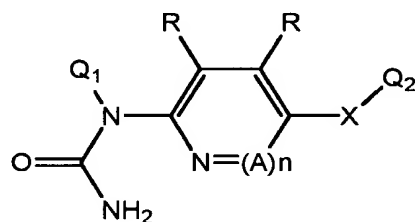
B<sup>7</sup> 37. (Amended) The method according to claim 26, wherein said method is used to treat an angiogenic disorder selected from solid tumors, ocular neovascularization, or infantile haemangiomas.

Sub C<sup>5</sup> 38. (Amended) A compound of the formula:

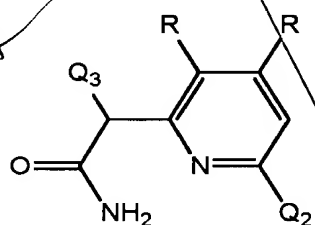
B



(Ie)

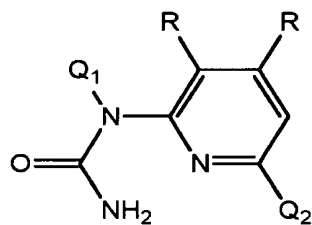


(If)



(Ig)

, or



(Ih)

wherein:

$Q_3$  is a 5-6 membered aromatic carbocyclic or heterocyclic ring system; or an 8-10 membered bicyclic ring system comprising aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein  $Q_3$  is substituted with 1 to 4 substituents, each of which is independently selected from halo;  $C_1$ - $C_3$  alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$  or  $CONR'_2$ ;  $O$ -( $C_1$ - $C_3$ )-alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$  or  $CONR'_2$ ;  $NR'_2$ ;  $OCF_3$ ;  $CF_3$ ;  $NO_2$ ;  $CO_2R'$ ;  $CONHR'$ ;  $SR'$ ;  $S(O_2)N(R')_2$ ;  $SCF_3$ ;  $CN$ ;  $N(R')C(O)R^4$ ;  $N(R')C(O)OR^4$ ;  $N(R')C(O)C(O)R^4$ ;  $N(R')S(O_2)R^4$ ;  $N(R')R^4$ ;  $N(R^4)_2$ ;  $OR^4$ ;  $OC(O)R^4$ ;  $OP(O)_3H_2$ ; or  $N=CH-N(R')_2$ ;

B

each of  $Q_1$  and  $Q_2$  are independently selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems, or 8-10 membered bicyclic ring systems consisting of aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein:

$Q_1$  is substituted with 1 to 4 substituents, independently selected from halo;  $C_1$ - $C_3$  alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$  or  $CONR'_2$ ;  $O$ -( $C_1$ - $C_3$ )-alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$  or  $CONR'_2$ ;  $NR'_2$ ;  $OCF_3$ ;  $CF_3$ ;  $NO_2$ ;  $CO_2R'$ ;  $CONHR'$ ;  $SR'$ ;  $S(O_2)N(R')_2$ ;  $SCF_3$ ;  $CN$ ;  $N(R')C(O)R^4$ ;  $N(R')C(O)OR^4$ ;  $N(R')C(O)C(O)R^4$ ;  $N(R')S(O_2)R^4$ ;  $N(R')R^4$ ;  $N(R^4)_2$ ;  $OR^4$ ;  $OC(O)R^4$ ;  $OP(O)_3H_2$ ; or  $N=CH-N(R')_2$ ; and

$Q_2$  is optionally substituted with up to 4 substituents, independently selected from halo,  $CH=N-OH$ , or  $CH=O$ ;  $C_1$ - $C_3$  straight or branched alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$ ,  $S(O_2)N(R')_2$ ,  $N=CH-N(R')_2$ ,  $R^3$ ,  $NH-CH_3$ ,  $NHCH_2CH_2OH$ ,  $NHCH_2CH(OH)CH_2OH$ ,  $CH_2OCH_2OCH_3$ ,  $NHCH_2CH_2NH_2$ ,  $NH$ -phenyl, piperazinyl, pyrrolidinyl or  $CONR'_2$ ;  $O$ -( $C_1$ - $C_3$ )-alkyl optionally substituted with  $NR'_2$ ,  $OR'$ ,  $CO_2R'$ ,  $S(O_2)N(R')_2$ ,  $N=CH-N(R')_2$ ,  $R^3$ , or  $CONR'_2$ ;  $NR'_2$ ;  $OCF_3$ ;  $CF_3$ ;  $NO_2$ ;  $CO_2R'$ ;  $CONHR'$ ;  $R^3$ ;  $OR^3$ ;  $NHR^3$ ;  $SR^3$ ;  $C(O)R^3$ ;  $C(O)N(R')R^3$ ;  $C(O)OR^3$ ;  $SR'$ ;  $S(O_2)N(R')_2$ ;  $SCF_3$ ;  $N=CH-N(R')_2$ ;  $CH=N-OH$ ;  $CH=O$ ; or  $CN$ ;

B

wherein R' is selected from hydrogen, (C<sub>1</sub>-C<sub>3</sub>)-alkyl; (C<sub>2</sub>-C<sub>3</sub>)-alkenyl or alkynyl; phenyl or phenyl substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl;

R<sup>3</sup> is selected from a 5-6 membered aromatic carbocyclic or heterocyclic ring system; and

R<sup>4</sup> is (C<sub>1</sub>-C<sub>4</sub>)-alkyl optionally substituted with N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', CON(R')<sub>2</sub>, or SO<sub>2</sub>N(R<sup>2</sup>)<sub>2</sub>; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with N(R')<sub>2</sub>, OR', CO<sub>2</sub>R', CON(R')<sub>2</sub>, or SO<sub>2</sub>N(R<sup>2</sup>)<sub>2</sub>;

X is selected from -S-, -O-, -S(O<sub>2</sub>)-, -S(O)-, -S(O<sub>2</sub>)-, N(R<sup>2</sup>)-, -N(R<sup>2</sup>)-S(O<sub>2</sub>)-, -N(R<sup>2</sup>)-C(O)O-, -O-C(O)-N(R<sup>2</sup>), -C(O)-, -C(O)O-, -O-C(O)-, -C(O)-N(R<sup>2</sup>)-, -N(R<sup>2</sup>)-C(O)-, -N(R<sup>2</sup>)-, -C(R<sup>2</sup>)<sub>2</sub>-, -C(OR<sup>2</sup>)<sub>2</sub>-, -CH(OH)-;

each R is independently selected from hydrogen, -R<sup>2</sup>, -N(R<sup>2</sup>)<sub>2</sub>, -OR<sup>2</sup>, SR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O<sub>2</sub>)-N(R<sup>2</sup>)<sub>2</sub>, or -C(O)-OR<sup>2</sup>, wherein two adjacent R are optionally bound to one another and, together with each Y to which they are respectively bound, form a 4-8 membered carbocyclic or heterocyclic ring;

R<sup>2</sup> is selected from hydrogen, (C<sub>1</sub>-C<sub>3</sub>)-alkyl, or (C<sub>1</sub>-C<sub>3</sub>)-alkenyl; each optionally substituted with -N(R')<sub>2</sub>, -OR', SR', -C(O)-N(R')<sub>2</sub>, -S(O<sub>2</sub>)-N(R')<sub>2</sub>, -C(O)-OR', or R<sup>3</sup>;

Y is C;

A is CR'; and

B

*82*  
*sub*  
*C5*  
n is 1; wherein an aromatic heterocyclic ring system  
comprises 1-2 heteroatoms independently selected from N, O or  
S.

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*B*



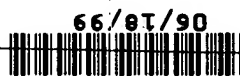


2

APPLICANT: GUY W. BEMIS ET AL

VIP/96-16 CIP2

TITLE: INHIBITORS OF p38



PAGES OF APPLICATION 125

NUMBER OF CLAIMS 37 SHEETS OF DRAWING

DECLARATION: ☒ EXECUTED ☐ UNEXECUTED

CHECK IN THE AMOUNT OF \$936.00

ASSIGNMENT RECORDATION FORM COVER SHEET

ASSIGNMENT & CHECK IN THE AMOUNT OF \$40.00

VERIFIED STATEMENT OF SMALL ENTITY STATUS

Receipt is hereby acknowledged of the above

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